



## Prevalence of a History of Testicular Cancer in a Cohort of Elderly Twins

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**Abstract.** Prior studies have suggested that the risk of testicular cancer among dizygotic twins may exceed that among monozygotic twins or the general population. Cryptorchidism is associated with testicular cancer and twinship, and therefore might potentially explain the findings of the prior studies. In 1993-1994, when they were 66 to 77 years of age, 14,326 twin individuals in the National Academy of Sciences-National Research Council Twin Registry were interviewed by telephone. A history of testicular cancer was reported by 5 (0.08%) of 5951 monozygotic twins and 11 (0.16%) of 6992 dizygotic twins. Follow-up interviews concerning testicular cancer risk factors and treatment were able to be administered to 4 of the monozygotic and 9 of the dizygotic twins reporting testicular cancer. A history of cryptorchidism was reported in the follow-up interview by only one dizygotic twin. Our data agree with the results of prior studies reporting a more frequent occurrence of testicular cancer among dizygotic than monozygotic twins. Although somewhat limited by small numbers, our study also suggests that the findings of increased testicular cancer in dizygotic twins are not explained simply by increased occurrence of cryptorchidism in twins.

**Key words:** Twins, Cancer, Testis, Cryptorchidism

## INTRODUCTION

In the United States, testicular cancer is the most frequently diagnosed cancer in men ages 20 to 34 years [13]. The incidence of the disease has risen almost continuously for at least the last two decades [14]. It is estimated that 7,100 new cases will be diagnosed in 1995 [19].

Cryptorchidism is the only known specific risk factor that is commonly associated with testicular cancer; however, only about 10% of men with the disease have or have had an undescended testis [15]. The etiology of the balance of cases is largely unknown.

It has been suggested that elevated estrogen levels in pregnancy might increase the risk of testicular cancer in sons [16]. Because maternal estrogen levels are elevated in twin compared to singleton pregnancies [8, 6, 1, 18], and these levels may be more elevated in dizygotic than monozygotic twin pregnancies [10], investigation of the incidence of testicular cancer among twins has been an approach to evaluating the potential effect of elevated levels of prenatal estrogens on testicular cancer.

A cohort study of US twin veterans of World War II found that the number of testicular cancer deaths among dizygotic twins exceeded the expected number and that this observed to expected ratio was almost double that among monozygotic twins, although the number of deaths was small and the differences were not statistically significant [4]. Another study reported the incidence of testicular cancer among the population-based Swedish twin registry [3]. The risk of testicular cancer among dizygotic twins younger than age 35 years was approximately 50% higher than among monozygotic twins and was also more than double that of the general population in Sweden.

The findings of the studies noted above could potentially be confounded by cryptorchidism because it is associated with testicular cancer and might be associated with twinship [2]. A very large telephone survey of World War II veteran twins provided a unique opportunity to assess whether twins reporting a history of testicular cancer also had a history of cryptorchidism or other factors that might be associated with testicular cancer.

## METHODS

Detailed descriptions of the creation of the National Academy of Sciences-National Research Council Twin Registry have been published [9, 11]. In brief, a search of birth certificates identified white male twins born in the United States from 1917 to 1927. Of the estimated number of twin births during that period, 93% were ascertained. Of these, the Veterans Administration Master Index file indicated that, during the World War II era, 15,924 twin pairs had served in the United States armed forces. The NAS-NRC Twin Registry is composed of these veterans. Zygosity determination, described in detail elsewhere, has been validated with blood testing and is estimated to be approximately 95% accurate [11].

In 1993 and 1994, telephone interviews were conducted for 14,326 twin individuals in the NAS-NRC Twin Registry. Ongoing mortality surveillance using Veterans Administration files suggests that more than 70% of the living twins (or their proxies) were interviewed [12]. Subject areas covered in the interview related primarily to neuro-psychiatric status; however, two questions about cancer were also included. Each twin was asked, "Did a doctor ever tell you that you had cancer?". If an affirmative response was provided, it was followed with "What type of cancer, that is, in what part of your body did the cancer start?". Sixteen subjects, who responded that they had been diagnosed with testicular cancer at some time in the past, were telephoned a second time. They were then asked more detailed questions to confirm the diagnosis of testicular cancer and to learn about known and possible testicular cancer risk factors, particularly cryptorchidism. One monozygotic and two dizygotic twins, who reported in the first telephone questionnaire that they had been diagnosed with testicular cancer, were unreachable by tele-

phone for the follow-up telephone interview. In addition, none of the three responded to registered letters requesting their further participation in our study.

Statistical significance of differences in proportions were assessed using the Mantel-Haenszel chi square test [5].

## RESULTS

A history of testicular cancer was reported in telephone interviews for 5 (0.08%) of 5951 monozygotic twins and 11 (0.16%) of 6992 dizygotic twins. The proportion among monozygotic twins was twice that among dizygotic twins; however, the difference did not achieve statistical significance ( $p = 0.24$ ).

The mean ages of the monozygotic and dizygotic twins reporting a history of testicular cancer were 48 years (range 26 to 65 years) and 42 years (range 20 to 69 years), respectively. All responding twins indicated that their testicular cancer had been treated surgically. None of the monozygotic twins and only one (11%) of the nine dizygotic twins contacted indicated a history of cryptorchidism. None of the responding twins provided a history of mumps orchitis. One of the dizygotic twins reported a history of hydrocele, and another dizygotic twin reported having had a hernia repair at age 5. None of the twins reported being left-handed.

## DISCUSSION

The data we report agree with the findings of two prior studies that reported a more frequent occurrence of testicular cancer in dizygotic than monozygotic twins [3, 4]. Cryptorchidism, although clearly linked to testicular cancer, does not fully explain the excess of testicular cancer observed in our study. Similarly, cryptorchidism might not explain the similar excesses observed in the prior studies. It is possible, however, that an underlying, but presently unknown, agent could cause or contribute to both cryptorchidism and testicular cancer.

In our study, one dizygotic twin with a history of testicular cancer reported having had a hernia repair at age 5 years and another had a history of hydrocele. Although suspected of being testicular cancer risk factors these conditions have not been clearly linked to testicular cancer [7] and their expected background prevalence in the population we studied is unknown.

Larger studies of twins could be expected to shed further light on the issues we have raised. However, testicular cancer is a relatively rare cancer, with an age-adjusted annual incidence of 4.4 per 100,000 US men in 1991 [13]. Twin births are also uncommon, representing about 2% of livebirths [17]. As a result of the rarity of testicular cancer and twinning, the study of their joint occurrence can be expected to be hindered by the problem of small numbers.

Taken together with prior studies, our findings are consistent with a role for prenatal factors (including hormones) in the etiology of testicular cancer. Our data, although limited by small numbers, also suggest that the findings of increased testicular cancer in DZ twins are not explained simply by increased occurrence of cryptorchidism in twins. An attempt to replicate our findings in a larger study would be useful to elucidate further the etiology of testicular cancer.

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